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From the Author.

ON THE KOMBÉ ARROW-POISON (STROPHANTHUS HISPIDUS, D. C.) OF AFRICA.

By Dr Thomas R. Fraser.

[The author communicated the results of some experiments with this poison to the Royal Society of Edinburgh, on the 21st of February, 1870; and an abstract of this communication has been published in the *Proceedings* of the Society (Vol. VII. No. 81, 1869—70, p. 99). As the circulation of these proceedings is, however, in great part limited to the Fellows of the Society, the author has thought it proper to reprint the abstract of his communication in a *Journal* where it will have the advantage of a wider and more general circulation.

In the following paper the abstract referred to will be reproduced *verbatim*, but a number of interpolations, consisting chiefly of details of experiments, will be introduced, in order to supply various omissions, many of which were rendered necessary by the original form of publication.

These interpolations will be included within brackets, so that they may be distinguished from the original abstract. The author has made no experiments with this substance since that abstract was published; he, however, entertains the hope of continuing the investigation.]

In nearly every narrative of exploration in uncivilised tropical regions, accounts are given, often no doubt somewhat fanciful, of poisonous substances which are said to possess the most remarkable properties. Usually these poisons are of vegetable origin; and the great majority may be included in the two divisions of *ordeal* and of *arrow* poisons, according as they are applied to one or other of these purposes. Among the most remarkable of the *ordeal-poisons* are the *Tanghinia venifera* of Madagascar, the *Physostigma venenosum* of Old Calabar, and the Akazga poison of the Gaboon; and of the *arrow-poisons*, the famous Curara or Wourali of South America, and the *Antiaris toxicaria* of Java.

The examination of these substances has not only proved of great value to physiology, but practical medicine has likewise been benefited—one of them, at least, being now an important medicinal agent.

In bringing before the Society a few of the results of a recent examination of a new arrow-poison, the author has to express his gratitude to the President, who very kindly gave him the specimens with which the experiments have been made. These specimens, consisting of a number of ripe follicles, were sent to Dr Christison by Mr Walker, and were collected in the expedition of the late Bishop Mackenzie.

Several specimens of the poison have likewise been sent to Professor Sharpey by Dr Kirk, H.M. consul at Zanzibar. Dr Kirk states "that the plant is a woody climber, growing in the forest, both of the valley and hills, and found at various places between the coast and the centre of the continent, above the Victoria Falls of the Zambesi. The stem is several inches in diameter, and rough outside. The plant climbs up the highest trees, and hangs from one to the other like a bush-vine. The flowers are of a pale yellow, and last for but a short time during the months preceding the first rains of the season (October and November). The fruit is ripe in June, and collected by the natives, who separate the rough outer coat before drying it, preserving the more leathery inner covering and the seeds[1]."

Dr Livingstone gives some interesting information regarding the poison in his *Narrative of an Expedition to the Zambesi and its Tributaries.* He mentions that arrows poisoned with it are used for killing wild animals only; arrows destined for the more noble object of killing men being poisoned with the entrails of a small caterpillar. Dr Livingstone says that in hunting, the natives follow the game with great perseverance and cunning: "The arrow, making no noise, the herd is followed until the poison takes effect, and the wounded animal falls out; it is then patiently watched till it drops; a portion of meat round the wound is cut away, and all the rest eaten" (p. 465).

[1] Extract from letter to Professor Sharpey, dated January 1, 1864.

Dr Livingstone also says that the poisoned arrows are made in two pieces. "An iron barb is firmly fastened to one end of a small wand of wood, ten inches or a foot long, the other end of which, fined down to a long point, is nicely fitted, though not otherwise secured, in the hollow of the reed which forms the arrow-shaft. The wood immediately below the iron head is smeared with the poison. When the arrow is shot into an animal, the reed either falls to the ground at once, or is very soon brushed off by the bushes; but the iron barb and poisoned upper part of the wood remain in the wound. If made in one piece, the arrow would often be torn out, head and all, by the long shaft catching in the underwood, and striking against trees" (p. 466)[1].

[It would appear that this arrow-poison is widely distributed over Africa, for it has been found not only at Kombé, on the west coast near the equator, and in the Manganja country, near the Zambesi at the south-east of Africa, but also in the Gaboon district[2], in Guinea[3], and in Senegambia[4]. In the Gaboon district it seems to be called Inée, Onaye, or Onage[5].]

The follicles examined by the author vary in *length* from about nine and three-fourths to about twelve and one-fourth inches, and in greatest *thickness* from about one inch to three-fourths of an inch, and they vary in *weight* from about 130 to 330 grains. They contain from 100 to 200 seeds, each of which weighs about half-a-grain, and has attached to it a beautiful comose appendix, placed on an extremely brittle stalk. For the identification of the plant the author is indebted to Professor Oliver of Kew, who writes, in a letter dated 10th Dec. 1869: "I reopen your note to say that I have just dissected a flower, and conclude to name the Kombé plant *Strophanthus hispidus*, D.C.[6]" This plant belongs to the natural order *Apocynaceæ*.

[1] Specimens of these arrows, which had been presented to Professor Maclagan by Dr Kirk, were exhibited to the Society.

[2] Pélikan, *Archives Générales de Médecine*, Juillet, 1865, p. 115.

[3] Van Hasselt, *Archives Néerlandaises des Sciences*, T. VII. 2me. Liv. 1872, p. 161.

[4] Baillon, quoted by Polaillon and Carville, *Archives de Physiologie*, No. 5, 1872, p. 526.

[5] Baillon, *loc. cit.*

[6] [Since this letter was received, Professor Oliver has been led, by a further

When the seeds contained in these follicles are bruised and treated in a percolator with rectified spirit, a greenish-yellow tincture is obtained. By distilling off the greater part of the spirit, and drying the residue on a water-bath and in the exhausted receiver of an air-pump, an extract is procured which weighs about 25 per cent. of the seeds employed, has an intensely bitter taste, and contains about one-half of its weight of an inert fixed oil[1]. From this extract the author has succeeded in separating a very powerful active principle. [He proposes that this active principle should be named strophanthin.]

As, however, the greater number of the experiments have been made with the extract, the results of these experiments only will be described in the following brief account of the physiological action of the Kombé arrow-poison, it being understood that the action of the active principle is of the same character.

When a small dose (one-twentieth of a grain) of this extract is mixed with a few minims of water, and injected under the skin of a frog, no distinct symptom is seen until about half-an-hour, when the animal's movements become somewhat sluggish. Soon afterwards the respirations cease, some stiffness occurs in the thoracic extremities, reflex sensibility diminishes, some stiffness appears in the pelvic extremities, and in about two hours after the administration voluntary movements entirely cease, and strong galvanic irritation produces no effect, even when applied to exposed muscles and nerves. An examination of the heart shows that it is completely paralysed, the ventricle being pale and contracted, while the auricles are dark and distended.

[To illustrate more fully the general symptoms that appear in frogs, the following experiment may be described :—

22*nd January*, 1870. 1.28 P.M. One-tenth of a grain of extract of strophanthus, suspended in 3 min. of distilled water, was injected under the skin at the left flank of a frog, weighing 287 grains. A

examination of the botanical characters of the Kombé-poison plant, to doubt its identity with *S. hispidus;* and, accordingly, he has described it in the Icones Plantarum, No. 4, 1870, under the name of *S. Kombé.*]

[1] [Microscopic examination shows that this extract contains a large number of acicular crystals; and when the fatty matters are removed from it by ether, a hygroscopic substance is obtained, which consists in great part of crystals.]

small quantity was lost, owing to the adhesion of the fatty matter to the syringe:—1.36. The frog is less active in moving and jumping about; but the limbs retain a normal position:—1.43. When irritated, it jumps feebly:—1.47. The thoracic extremities are weak, and the thorax often rests on table:—1.56. The frog is on the abdomen and thorax; when irritated, pretty energetic movements occur of the four extremities, but the frog does not jump, although it obviously intends to do so. The respiratory movements of the throat are shallow, and those of the flanks are very feeble and occur only rarely:—2.8. A good deal of frothy mucus has been exuded; there is no exaggeration of the reflex excitability:—2.12. Almost incessantly, fibrillary twitches are occurring in the muscles of the abdomen. Both throat and chest respirations have ceased:—2.25. When placed on the back the frog attempts to turn, but cannot do so. No cardiac impulse can be detected. The fibrillary twitches continue, and are best seen at the lumbar region and behind the eyeballs. When the skin is irritated, pretty energetic movements occur in the two pelvic extremities and in the abdominal walls, and only feeble movements in the thoracic extremities:—2.45. Irritation of the skin causes feeble reflex movements in the two pelvic extremities; but none in the thoracic, which are now stiffly extended at right angles to the body. The fibrillary twitches no longer occur spontaneously; when, however, the skin at the coccyx or upper part of the thigh is irritated, a series of fibrillary twitches follow at the lumbar and gluteal regions:—2.55. Galvanic stimulation of the muzzle excites feeble reflex movements in the pelvic extremities, but none elsewhere:—3.10. Weak galvanic stimulation excites no movement; a very strong galvanic current, however, still excites extremely feeble movements in the pelvic extremities. The four extremities are now stiff and extended:—3.12. The heart was exposed, and it was found to be motionless, with the ventricle contracted and white, and the auricles distended and dark. Even the most powerful galvanic current from a Daniel's cell and Du Bois Reymond's induction apparatus, applied directly to its surface, produced no movement whatever:—3.30. Galvanic stimulation of the exposed right sciatic nerve caused only some very feeble and sluggish movements of the right foot. Strong galvanic stimulation of the exposed muscles of the right thigh failed to produce any contraction:—3.50. Galvanic stimulation of the right sciatic nerve no longer produces any effect. When the muscles of various parts of the body are stimulated, no movement occurs. A certain degree of general stiffness is present, and the four limbs continue extended:—*23rd January*, 12.50 P.M. Strong general rigor. The ventricle of the heart is contracted and white; the auricles are distended with blood.]

It was obviously suggested by these phenomena that this substance acts as a cardiac poison; and, accordingly, some experiments were made in which the heart was exposed before the administration, of which the following is an example:—

One-tenth of a grain of extract was injected under the skin of a frog. Five minutes thereafter, it was observed that the ventricular systole was somewhat prolonged; in six minutes, the ventricular diastole was imperfect, so that only portions of the ventricle dilated to admit blood from the auricles; in six minutes and thirty seconds, the greater portion of the ventricle was continuously pale and contracted, each auricular systole propelling merely a small drop of blood into the ventricle, where it produced a dark, pouch-like projection, which at times disappeared, and at other times only changed its position during the imperfect systole of the ventricle; in seven minutes, the ventricle altogether ceased to contract, while the movements of the auricles continued at nearly the normal rate; and in eighteen minutes, the auricles in their turn became motionless, but, in place of being contracted and empty like the ventricle, they were distended and full of dark blood. Notwithstanding this absolute paralysis of the heart, respiratory movements occurred for twenty-five minutes after the ventricle had ceased to contract, and the frog jumped about actively for some time after this.

[In many other experiments, the heart was exposed before strophanthus was administered, but only the two following will be here described. In the first, the poison was administered by the stomach, and in the second, by the rectum.

15*th January*, 1870. A frog, weighing 310 grains, was secured in the usual way. 11.54 A.M. The heart was exposed by removing the sternum:—11.56. Heart's contractions, 13 per 30 sec.:—11.59. Heart's contractions, 13 per 30 sec.:—12. A narrow gum elastic tube was passed into the stomach:—12.3. 0.2 grain of extract of strophanthus, suspended in 8 min. of distilled water, was injected down the tube into the stomach. Almost immediately violent efforts to vomit occurred, and a portion of the fluid was ejected:—12.6. Heart's contraction, 15 per 30 sec.:—12.7. "Pouching" observed at the heart's apex:—12.9. Heart's contractions, 14 per 30 sec.:—12.10. Heart's contractions, 14 per 30 sec.:—12.13. Heart's contractions, 15 per 30 sec.:—12.18. Heart's contractions, 15 per 30 sec.:—12.25. Heart's contractions, 15 per 30 sec.:—12.32. Imperfect ventricular diastole; a portion only of the ventricle dilating during diastole, and an appearance of "pouching" being thereby produced:—12.33. No diastole of ventricle, but a movement of that cavity occurs at times, although systole is continuously maintained:—12.35. A number of ventricular contractions, with diastolic dilatations in proper rhythm during 20 seconds, and, then, only movements of the ventricle without diastole:—12.36. No movements of ventricle, systolic contraction being continuously maintained. The auricles contract regularly 13 times per 30 sec.:—12.50. Auricular contractions, 6 per 30 sec. No movement of ventricle:—12.55. Auricular contractions have ceased: the auricles are dark and distended, and slight movements may be occasionally excited in them by direct irri-

tation; the ventricle is pale and contracted, and no movement occurs when the surface is irritated:—12.58. The frog was unfastened, and it jumped about with considerable activity:—1.30. The frog is jumping and moving about, but less actively, and a little stiffness is present in the thoracic extremities. The heart is perfectly motionless:—1.50. Ditto:—2.45. The frog no longer moves about, and it is lying on the abdomen and chest with the lower jaw resting on the table. Reflex movements can be readily excited, but they are sluggish. The limbs are somewhat stiff:—16*th January*. 3 P.M. General rigor. No contractions can be excited by stimulating the nerves or muscles.

20*th January*, 1870. 2.25 P.M. The heart of a frog, weighing 330 grains, was exposed in the usual way, the frog being secured on the back:—2.28. Heart's contractions, 12 per 30 sec., regular and rhythmical:—2.30. Heart's contractions, 12 per 30 sec.:—2.31. Heart's contractions, 12 per 30 sec.:—2.34.30. Injected 0.1 grain of extract of strophanthus, suspended in 2 min. of distilled water, into the rectum, by means of a gum elastic tube attached to the orifice of the hypodermic syringe; and, afterwards, injected 1 min. of distilled water. A little of the fluid escaped:—2.40. Heart's contractions, 12 per 30 sec.:—2.45. Heart's contractions, 12 per 30 sec.:—2.48. Heart's contractions, 12 per 30 sec.; imperfect, the diastole being only partial at the apex:—3.10. Heart's contractions, 12 per 30 sec. The respirations continue:—3.17. Heart's contractions irregular; there being 5 ventricular contractions per 30 sec., and 3 auricular contractions to each ventricular contraction. The ventricle remains contracted during two auricular beats:—3.20. Ventricular contractions, 7 per 30 sec.; and 2 auricular contractions occur for each ventricular contraction:—3.23. Ditto. The respirations continue, and the frog often struggles:—3.24. Ditto. The ventricular diastole is imperfect, the upper half of the ventricle remaining contracted continuously, while diastole occurs at the apex only:—3.26. 6 imperfect ventricular and 12 perfect auricular contractions per 30 sec. The upper two-thirds of the ventricle now remains continuously contracted (in systole), and only the lowest third dilates during diastole. The diastole of the ventricle consists, therefore, of a mere "pouching" of the lowest third; and it is very brief in duration, being almost immediately followed by contraction (systole) of that third, which continues during two auricular contractions:—3.29. 6 imperfect ventricular contractions per 30 sec.; the appearance of a small dark "pouch" at the apex, and the occasional and rare appearance of a small "pouch" at the left base constituting its diastole. Auricular contractions, 12 per 30 sec., regular. Respirations continue, and, occasionally, there are general struggling movements:—3.32. 4 imperfect ventricular contractions per 30 sec., limited to the formation of a minute dark "pouch" at the apex. Auricular contractions, 12 per 30 sec., regular:—3.34. Only at long intervals a feeble movement occurs in the ventricle; which is now altogether permanently contracted and pale. Auricular contractions, 10 per 30 sec.:—3.35. No movement of ventricle. Auricular contractions, 6 per 30 sec.; at times, there is a long pause:—

3.37. On two occasions since last note, one imperfect ventricular movement occurred, following the formation of a minute dark "pouch" at the apex. Auricular contractions, 9 per 30 sec.:—3.39. Auricular contractions, 8 per 30 sec. One imperfect ventricular contraction during every three auricular contractions; a pouch forming at the apex at the second of the three auricular systoles, and being emptied immediately after the third:—3.43. Auricular contractions, 7 per 30 sec. No movement of ventricle, which is contracted and pale:—3.45. Ditto. Occasional gasping respirations:—3.50. Auricular contractions, 6 per 30 sec., feeble and irregular:—3.51.30. Auricular contractions have ceased; the auricles are dilated and dark, and the ventricle is contracted and white. Occasionally gasping respirations occur:—3.54. Ditto. Irritation of the surface of the ventricle causes a slight, almost doubtful, movement; while irritation of the surface of the auricles causes a series of contractions limited to the auricles and continuing for one minute, when they ceased after some struggles on the part of the frog:—3.57. Irritation of the surface of the ventricle produces no effect; and of the surface of the auricles, a single contraction followed by complete rest:—4.7. Galvanic irritation, even when powerful, applied to various portions of the ventricle and auricles produces no movement of the heart, but it excites violent struggles:—4.9. The frog was set free. It assumed a nearly normal posture, excepting that the thoracic extremities were extended and somewhat stiff; and, although able to move about pretty actively, it cannot jump:—4.30. Irritation of the skin caused pretty active reflex movements of the four limbs, but afterwards, one pelvic extremity remained extended in a rather stiff condition:—21*st January*, 11 A.M. General rigor: muscles hard and pale; veins full of blood, arteries empty; ventricle pale with some red patches, auricles dark and dilated.

In the last two experiments the heart was affected much more gradually than when strophanthus is subcutaneously injected; and the changes that take place in its action were, therefore, exhibited in a very distinct manner.]

The experiments that have been performed with birds and mammals have likewise shown that this poison acts primarily on the heart.

[By way of illustration, a few particulars may be given of an experiment on a pigeon, and of one on a rabbit.

9*th February*, 1870. 4.5 P.M. One-tenth of a grain of extract of strophanthus was suspended in 4 min. of distilled water, and injected under the skin at the right side of a healthy pigeon, weighing ten ounces:—4.12. The pigeon vomited a large number of entire wheat grains:—4.13. Ditto:—4.15. Ditto. Some mucous substance is also vomited. There is decided feebleness of the limbs:—4.20. Frequently

vomited since last note, and some liquid excrement is now passed:—4.22. The pigeon is lying on the abdomen, the wings being used to steady the body. The pupils are dilated:—4.23. Some spasms occurred, which have an opisthotonic character:—4.23.30. Respirations have ceased. The pigeon is dead:—4.24.30. The heart was exposed and found to be motionless:—4.28. Direct galvanic stimulation of a sciatic nerve caused active muscular contractions:—4.30. Galvanic stimulation, even when powerful, applied to the surface of the heart produced no movement. Galvanic stimulation, applied to the muscles of the limbs and body, produced active contractions. The pupils are still dilated:—5.5. The muscles of the body no longer contract under galvanic stimulation; and they have become somewhat hard.

5th February, 1870. In an active rabbit, weighing 4 lbs. 2 oz., it was found that at 4.45 P.M. the respirations occurred 42 times, and the cardiac impulse 49 times, per 10 sec.; while the pupils measured $\frac{15}{50} \times \frac{13}{50}$ of an inch:—4.50. Two-tenths of a grain of extract of strophanthus, suspended in 10 min. of distilled water, was injected under the skin at the left flank:—4.53. Respir. 43 per 10 sec. The animal is restless:—4.57. Card. imp. 41 per 10 sec. Right pupil, $\frac{15}{50} \times \frac{13}{50}$ of an inch:—4.58. Respir. 47 per 10 sec.:—4.58.30. Card. imp. 35 per 10 sec.:—4.59. Respir. 39 per 10 sec.:—4.59.30. Card. imp. 39 per 10 sec.:—5.1. Card. imp. 39 per 10 sec. Grinding movements of the teeth:—5.2. Respir. laboured, and a sharp sound (like a "smack") occurs with them:—5.3. Card. imp. 35 per 10 sec.; the impulse is greatly reduced in strength:—5.4. Respir. 9 per 10 sec. Right pupil, $\frac{15}{50} \times \frac{13}{50}$ of an inch:—5.5. Card. imp. 35 per 10 sec. The sounds continue to occur with the respiratory movements:—5.6. Respir. 10 per 10 sec. Right pupil, $\frac{14}{50} \times \frac{13}{50}$ of an inch:—5.7. Card. imp. cannot be counted accurately, but it seems to occur about 38 times per 10 sec.:—5.8. Respir. 13 per 10 sec., no longer accompanied with any sound:—5.10. Respir. 23 per 10 sec.:—5.11. Card. imp. 41 per 10 sec., again distinct:—5.14. Card. imp. 38 per 10 sec. The rabbit is in a somewhat crouching posture:—5.14. Respir. 23 per 10 sec., jerking in character:—5.16. Card. imp. 39 per 10 sec.:—5.18. Respir. 26 per 10 sec.:—5.18.30. Card. imp. 38 per 10 sec. The lips and mouth are frequently opened and shut. Usually the eyelids are nearly closed:—5.22. Respir. 24 per 10 sec., jerking. The rabbit is unsteady, and tends to fall over:—5.23.30. Card. imp. 40 per 10 sec.:—5.25. The rabbit is now sitting, and the head often falls slowly and is raised sharply, with nodding movements:—5.26. Respir. 13 per 10 sec., feeble and jerking:—5.26.30. Card. imp. 33 per 10 sec. Right pupil, $\frac{14}{50} \times \frac{13}{50}$ of an inch:—5.30. Respir. 8 per 10 sec. Frequent shaking movements of the head:—5.32. Card. imp. cannot be counted, because of the jerking respiratory movements, and of frequent tremors; but it seems to occur about 24 times per 10 sec.:—5.34. Respir. 14 per 10 sec. Incessant tremors, chiefly of the head:—5.38. The rabbit is lying flaccidly, with the lower jaw resting on the table. Tremors occur frequently; and occasionally somewhat spasmodic movements take place, during which the body is tossed about:—5.41. Respir. 7 per 10 sec. The rabbit lies quietly on the

side:—5.42. Card. sounds (as heard by the stethoscope) are very feeble and irregular. Right pupil, $\frac{10}{50} \times \frac{8}{50}$ of an inch:—5.42.30. Occasionally a gasping respiration occurs. Right pupil, $\frac{18}{50} \times \frac{17}{50}$ of an inch:—5.43. No respiratory movements; conjunctiva and cornea are insensible. The rabbit is dead:—5.44. No card. imp. can be felt, nor sound heard with the stethoscope:—5.46. The right sciatic nerve was exposed: weak galvanic stimulation produced no effect when applied to it, or to the surfaces of the exposed muscles in the gluteal region; but very strong stimulation when applied to the nerve excited a faint twitch of the foot, and when applied to the exposed muscles, a slow and feeble contraction. These conditions were present also at 5.50:—5.48. Right pupil, $\frac{8}{50} \times \frac{7}{50}$ of an inch:—5.52. The heart was exposed, and found to be motionless; while stimulation, even when powerful, produced no effect upon it:—5.55. Galvanic stimulation of nerves and muscles no longer produces any effect. The intestinal peristalsis is observed to be very slight:—6.30. General rigor, not very strong, except in the pelvic extremities. Right pupil, $\frac{8}{50} \times \frac{7}{50}$ of an inch.

Experiments were also made with dogs and cats, and results similar to the above were obtained.]

An endeavour was made to ascertain by what mode of action these very peculiar cardiac effects are produced. With this object experiments were made, in which the cerebro-spinal axis was completely destroyed, in which the vagi nerves were divided, and in which the peripheral terminations of the vagi were paralysed by atropia, previously to the exhibition of the Kombé poison; but no important modifications were thereby caused, and it is therefore obvious that the action on the heart is not exerted through the cerebro-spinal nerves. In other experiments, after complete cardiac paralysis, the surface of the heart was irritated by galvanic and other stimulants, but no effect was thereby caused.

[It is, therefore, perfectly obvious that strophanthus exerts an action upon the heart, which is independent of any change that it may produce in the physiological condition of the cerebro-spinal nervous system and of its connections with this organ. It is also obvious that this substance *acts in a powerful and direct manner upon the cardiac muscular fibre;* greatly prolonging, in the first place, the contraction of those fibres, and, ultimately, rendering it continuous, and only to be overcome when relaxation occurs as a natural consequence of *post-mortem* decomposition. Whether the intra-cardiac nerves are

likewise affected, and whether a modification of their physiological activity is concerned in the production of these remarkable effects, it is extremely difficult to determine, seeing that their condition cannot readily be discovered in presence of so powerful and direct an action upon the muscular fibres that are controlled by them. The experiments that have as yet been made tend to show that the final stoppage of the heart and the production of the virtually permanent state of ventricular systole are independent of any modification that may be effected in the physiological condition of the intra-cardiac nerves. An example of these experiments may be here given.

19*th February*, 1870. 3.5 P.M. In a frog, weighing 361 grains, the heart was exposed:—3.9. Heart's contractions, 10 per 30 sec.:—3.14. Heart's contractions, 12 per 30 sec.:—3.16. Heart's contractions, 12 per 30 sec.:—3.17. One-twentieth of a grain of extract of strophanthus, suspended in a very little distilled water, was injected under the skin at each thigh (0.1 gr. in all):—3.20. Heart's contractions, 13 per 30 sec.:—3.21. Heart's contractions, 13 per 30 sec.:—3.23. Heart's contractions, 12 per 30 sec.:—3.24. Heart's contractions, 13 per 30 sec.; the ventricular systole is rather prolonged:—3.26. The ventricle no longer dilates; it is in a state of continuous systole:—3.28. Auricular contractions, 8 per 30 sec.; irregular:—3.29. Auricular contractions, 6 per 30 sec.; regular, but the diastole is only momentary:—3.32. Auricular contractions have ceased. Respir. 7 per 30 sec.:—3.34. The heart was removed from the thorax, by cutting the vessels at the base with a pair of scissors, and it was placed on a porcelain slab moistened with serum:—3.36. Galvanic stimulation, applied to various parts of the removed heart, produced no movement. The lower two-thirds of the ventricle was cut off with a pair of sharp scissors, and stimulated with galvanism, but without any effect—this separated portion remaining hard and contracted.

The data that have been acquired are not, however, sufficient to permit the assertion that no action is exerted upon the intra-cardiac nerves. It is by no means improbable that these nerves are directly acted upon; and that a modification in their physiological condition aids in producing the irregularities in the rhythm and the intermissions in the contractions of the heart, which occur during the earlier stages of the poisoning, and before the functional activity of the cardiac muscle has been destroyed.]

Another very prominent action of this poison is that exerted

on the voluntary muscles, by which their activity is gradually impaired, and finally completely destroyed, so that the muscles are quickly in a condition of true *rigor mortis*.

[The nature of this action has to a certain extent been described in the preceding experiments; it will, therefore, be sufficient to give a brief account of some of the experiments in which its mode of production was investigated.

It is shown by the following experiment that the effects on the striped muscles of the body do not result from the paralysis of the heart which strophanthus produces:—

12*th January*, 1870.

A.	*B.*
1.15. A frog, weighing 266 grains, was placed on its back, and secured. The heart was then exposed:—1.20. Heart's contractions, 12 per 30 sec.	
1.21.	The heart of a frog weighing 268 grains was exposed in the same way as in *A*.
1.23.	Heart's contractions, 12 per 30 sec.
1.25.	A ligature was drawn tightly round the base of the heart, so as completely to stop the circulation; pulsation continued, however, in the large vessels close to the heart.
1.31. One-tenth of a grain of extract of strophanthus was injected under the skin of the two thighs:—1.39. Ventricular contractions have ceased, and the ventricle is pale and contracted. Auricular contractions, 11 per 30 sec. and feeble:—1.45. Auricular contractions have ceased:—1.46. The frog was set free: it jumped about actively:—1.49. The thoracic extremities are a little stiff, though still mobile. The frog can no longer jump, but it pushes itself about by vigorous movements of the pelvic extremities.	
1.50.	The frog is set free, and jumps about actively.

2. The thoracic extremities are very stiff. Irritation produces pretty active reflex movements of the pelvic extremities. Twitches occur at the lower part of the abdominal wall. Respir. has ceased.

2.10. ... ... The frog continues to jump about actively.

2.25. Irritation of the skin produces no movement, unless it be powerful, when slow but strong reflex movements occur in the pelvic extremities, but only at a considerable interval after the application of the irritant.

2.30. ... ... The frog jumps only feebly when irritated. Active spontaneous movements, however, still occur.

2.34. The pelvic extremities are now somewhat stiff, and when the skin is irritated very sluggish and feeble reflex movements occur in them. The twitches of the muscles have ceased.

2.35. ... ... The frog jumps spontaneously.

2.37. Strong galvanic stimulation applied to any part of the skin produces no effect, except when it is applied to one of the feet, when feeble movements occur slowing, which are strictly localised to the parts through which the galvanic current is passed. Galvanic stimulation applied to the exposed left sciatic nerve produces feeble movements below the left knee, but no reflex contractions:—2.52. Strong galvanic stimulation applied to the exposed sciatic nerve produces no contraction; when applied to exposed muscles in the left thigh and calf no movement whatever occurs.

3. ... ... The frog cannot now jump, but it pushes itself about by vigorously moving the four extremities.

4.15. ... ... The frog has for some time been lying on the abdomen, thorax, and lower jaw. Irritation causes well-marked reflex movements.

13*th January*, 1 P.M. ... ... Irritation no longer excites reflex movements. Galvanic stimulation of an exposed sciatic nerve causes only feeble movements of the limb supplied by the nerve; but it causes active contractions in the muscles, when directly applied to their surface. The body and limbs are perfectly flaccid.

1.5. General rigor is present everywhere; and the muscles are hard and pale. The ventricle is pale and rigid:—16*th January*, 12.10 P.M. Ditto:—17*th January*, 1 P.M. Ditto:—18*th January*, 11 A.M. The muscles are now softer. The ventricle is less rigid, and at several places dark patches are seen.

That the action of strophanthus upon the striped muscles of the body is not the result of any influence conveyed to them by the spinal motor nerves is rendered apparent by the following experiment:—

28*th January*, 1870. 3.58 P.M. One-twentieth of a grain of sulphate of methyl-strychnium was dissolved in 4 min. of distilled water, and injected under the skin at the left flank of a frog, weighing 290 grains:—4.25. Galvanic stimulation of the skin does not produce any reflex movement:—4.35. Galvanic stimulation of the exposed left sciatic nerve does not produce any muscular contraction in the left pelvic extremity or elsewhere:—4.40. A ligature was passed below the left sciatic nerve, and tied tightly round the middle of the left thigh; the nerve, therefore, not being included within the ligature:—4.44. The frog was secured on the back, and the heart was exposed:—4.45. Cardiac contractions, 9 per 30 sec., regular and rhythmical:—4.47. One-tenth of a grain of extract of strophanthus, suspended in 3 min. of distilled water, was injected under the skin at the right flank:—5.44. Heart's contractions are irregular and non-rhythmical: the greater part of the ventricle being continuously contracted and white, and only a small dark pouch being formed during diastole, which is emptied after each alternate auricular contraction. Twitches occur in the muscles of the abdomen and upper part of right (non-ligatured) thigh:—5.52. The ventricle is now altogether motionless, and it is white and contracted. Occasionally some feeble movements occur in the auricles. The twitches of the muscles have ceased; and the thoracic extremities are stiff:—29*th January*, 3 P.M. The ventricle is contracted, its anterior surface is

pale, but its posterior is dark; and the auricles are dark and not distinctly contracted. Galvanic stimulation, applied to the heart, produces no effect. The thoracic extremities are stiff and hard; the right (non-ligatural) pelvic extremity is stiff, and the muscles at the thigh are hard, while those below the knee are less so. Galvanic stimulation of the muscles of the right pelvic extremity, or elsewhere in the poisoned region, produces no effect; but galvanic stimulation of the muscles (through the skin) of the left (ligatured) pelvic extremity produces active contractions in that extremity:—30*th January*, 4 P.M. Ditto:—31*st January*, 4 P.M. Contractions can no longer be produced in the left (ligatured) pelvic extremity by galvanic stimulation.

That the action of strophanthus upon the striped muscles of the body is the result of direct contact with these muscles is rendered apparent by the following experiment:—

24*th January*, 1870. 1.55 P.M. In a frog, weighing 350 grains, a ligature was tied tightly round the structures of the right thigh excepting the trunk of the right sciatic nerve:—2.3. The frog was secured on the back, and the heart was exposed:—2.4. Heart's contractions, 13 per 10 sec., regular and rhythmical:—2.9. One-tenth of a grain of extract of strophanthus, suspended in 2 min. of distilled water, was injected under the skin at the left flank:—2.19. Ventricular contractions, 13 per 30 sec., and imperfect; the middle zone of the ventricle remaining always in systole, and only the base and apex dilating in diastole:—2.21. Imperfect diastole of ventricle, 7 per 30 sec.; different limited portions become at different times pouched to constitute the diastole, and at times a drop of blood is distinctly seen to be conveyed from one part to another of the ventricle:—2.24. Ventricular contractions have altogether ceased, and the ventricle is contracted and white. Auricular contractions, 11 per 30 sec. The respirations continue:—2.34. Auricular contractions have ceased. Respiratory movements continue:—2.36. The frog was set free; and it moved about pretty actively:—2.50. Spontaneous jumps occur, but they are rather stiff. Both pelvic extremities are moved actively; but the left (non-ligatured) more so than the right (ligatured), the ligature round the right thigh having caused that limb to become a little extended:—3. Voluntary movements are feeble. Twitches occur in the left thigh. Respiration is represented by infrequent gasping movements:—3.14. Nearly constant slight twitches in the left (non-ligatured) thigh. The tone of the left pelvic extremity is impaired, as it now usually remains partially extended:—3.25. Slight irritation, applied anywhere, causes a series of movements in the body and four extremities, but these movements are now more active in the right (ligatured) pelvic extremity than in the left:—4.44. Galvanic stimulation, applied to the muzzle, causes reflex movements in the right (ligatured) pelvic extremity, but nowhere else:—5. Ditto. Galvanic stimulation applied to the sciatic nerve of the

left (non-ligatured) pelvic extremity causes movements of that extremity:—5.30. Galvanic stimulation of the sciatic nerve of the left (non-ligatured) pelvic extremity no longer causes any movement: but when applied to the sciatic nerve of the right (ligatured) pelvic extremity, above the ligature, it causes active movements of the right pelvic extremity; and when passed through the spinal cord it is followed by energetic movements of this extremity, and of no other part of the body. Galvanic stimulation, even when strong, of the muscles of the left pelvic extremity causes no contraction. It is found that a cut section of one of these muscles has an acid reaction. The muscles of the thoracic extremities are also non-contractile and acid in reaction:—6. Ditto. While the thoracic extremities are very rigid, and the left (non-ligatured) pelvic extremity slightly so, the right (ligatured) pelvic extremity is flaccid and its muscles are contractile and alkaline.]

Regarding the other physiological effects, it is sufficient briefly to mention that the sensory and motor spinal nerves, the abdominal and cervical sympathetics, and the muscular walls of the stomach, intestines, bladder, and uterus, are paralysed at an early stage, although not until the blood-heart had ceased to contract; while the lymph-hearts of the frog retain a normal rate, long after paralysis of the blood-heart[1].

From these results it is apparent, that the primary action of the Kombé arrow-poison is isolated in the heart, and that it may therefore be included in the class of the *cardiac poisons*,—a class of poisons whose action has been most accurately defined by the researches of Kolliker, Vulpian, Pélikan, Hammond and Weir Mitchell, Hilton Fagge and Stevenson, Holme, Dibkowsky, and others.

[The author believes that this preliminary investigation enables him to make the following statements:—1. Strophanthus acts primarily upon the heart, and produces, as the final result of this action, paralysis of that organ with permanence of the ventricular systole. 2. Pulmonary respiration continues in cold-blooded animals for several minutes after the heart is paralysed. 3. The striped muscles of the body are acted upon: twitches occur in them; their tonicity is exaggerated; and, finally, their functional activity is destroyed, the muscles being

[1] The author is indebted to Professor Sharpey of London for an account of some unpublished experiments made with this poison in 1862. The results mentioned in the above abstract harmonise in the most satisfactory manner with those obtained by Professor Sharpey.

then hard, and, soon afterwards, acid in reaction. These changes are accomplished subsequently to the final effect on the heart. They are the result of a direct contact of the substance with the muscles themselves, and are independent of the action on the heart, as well as of any changes that occur in the physiological condition of the cerebro-spinal nervous system. 4. The reflex function of the spinal-cord is suspended soon after the heart is paralysed; but the motor conductivity of the spinal-cord and of the nerve-trunks continues after the striped muscles of the body are paralysed. 5. The lymph-hearts of the frog continue to contract for many minutes after the blood-heart has been paralysed.]